Kenshalo, Daniel 2000

Dr. Daniel Kenshalo Oral History 2000

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Dr. Dan Kenshalo
March 17, 2000

Good morning. Today is the 17th of March in the year 2000, and we're (Marcia Meldrum) starting our interview with Dr. Dan Kenshalo in Building 49 on the NIH campus.

Meldrum: And Dr. Kenshalo, good morning.

Kenshalo: Good morning.

Meldrum: Why don't you begin by telling me a little bit about your background. You grew up in St. Louis.

Kenshalo: Tallahassee, Florida.

Meldrum: Tallahassee, Florida. You were born in St. Louis and you grew up in Florida. That sounds very, very nice.

Kenshalo: It was a comfortable environment.

Meldrum: So, tell me a little about your growing up. Your dad was a scientist.

Kenshalo: Yeah. He was a professor at Florida State University, in psychology. He was primarily interested in temperature sensitivity.

Meldrum: And so, physiological experiments.

Kenshalo: Mm-hmm, primary afferent recordings from thermoreceptors.

Meldrum: In monkeys?

Kenshalo: Monkeys, cats, did a lot of behavioral work as well in monkeys, psychophysics, humans and monkeys.

Meldrum: Were you a visitor to the lab at an early age or...

Kenshalo: Yes.

Meldrum: So this was really interesting.

Kenshalo: Mm-hmm. Used to go and help the graduate students do physiology.

Meldrum: Really?

Kenshalo: Yeah.

Meldrum: That's neat.

Kenshalo: Yeah, it was fun.

Meldrum: Yeah, so that's great. So, tell me a little bit about growing up in Florida. I mean, what were your other interests?

Kenshalo: Tennis.

Meldrum: Tennis.

Kenshalo: Tennis, always tennis. Still is.

Meldrum: So you were looking for a scientific job where you could play tennis.

Kenshalo: Could be.

Meldrum: And you grew up in Florida. And tell me about how your planning for your career sort of developed. Or was it serendipity, or what happened?

Kenshalo: I enjoyed doing the physiology, the physiological experiments, and working with the monkeys behaviorally and, just after that, went to graduate school. It was a logical consequence.

Meldrum: First you went to college.

Kenshalo: Right. I was an undergraduate at Florida State, worked in my father's lab, worked in a number of other labs. The last year at Florida State, I was exposed to a tremendous number of visiting scientists that came through.

Meldrum: Oh, wow, yeah. That's exciting.

Kenshalo: Yeah. Met a couple of Nobel laureates and things like that as a young kid who had no respect for those people at the time or knew what they were about, and that's how I got into science.

Meldrum: Okay. You were pretty much determined on a research career from the very beginning?

Kenshalo: Oh, yeah. I think so, definitely. That was always more fun than everything else, including academics.

Meldrum: Okay. So when you chose to go to graduate school, what factors played into your choice? You went to Georgia?

Kenshalo: Yeah. It was reasonably close.

Meldrum: That's true.

Kenshalo: And still in the South, still. My GRE grades were fairly reasonable but my grade point average wasn't spectacular at that point in time.

Meldrum: And while you were there, you worked for a while at Yerkes.

Kenshalo: Yes, the Yerkes Primate Center, in the field station working with...

Meldrum: I think that's a fascinating place.

Kenshalo: Yeah. It was--we worked on an Army contract that was looking at physiological correlates of dominance and submission in rhesus monkey troops, male rhesus monkey troops. And specifically we were looking just to see if we could find operant correlates that would predict whether an animal was going to be a high-ranking male or a low-ranking male. And we were responsible for training the monkeys and programming all the computers and doing things like that.

Meldrum: Okay, now, I mean, Fred's showing me how his setup was working. Is this the same? Were you training the monkeys primarily by behavioral cues? Were they being given--were they hooked up to things that would give them stimuli?

Kenshalo: Yes. Well, they were hooked up to things... Yeah, they would get various lights of various kinds and they would--we'd have various kinds of operant schedules that they'd have to perform on, like fixed-ratio scale, fixed-ratio schedules, and fixed-interval schedules and things like that, and see if they would be... Then the animals would be brought into the operant boxes daily and then they'd be tested for a couple of hours and put back in the social situation. And then we'd look to see if we could find any correlates between what was going on in the operant box and what was going on in their social hierarchy.

Meldrum: And did you?

Kenshalo: Yeah, but for the life of me, I can't remember what they were. I mean, I think... As I recall, higher-dominant animals tend to be more persistent in operant schedules than lower-ranking animals, for some reason. But there were a couple of papers that came out on that, but I don't remember what.

Meldrum: Yeah, there were a couple of papers.

Kenshalo: Twenty-five years ago, what they said...

Meldrum: I think that it was, if you put them on a--what--an intermittent reinforcement... That's not it.

Kenshalo: Fixed interval.

Meldrum: Fixed interval or something.

Kenshalo: Yeah.

Meldrum: That the lower-orders were more anxious to--they kept returning to the stimuli no matter what...

Kenshalo: Yeah.

Meldrum: Whereas the higher-orders seemed to be--this is my interpretation--more relaxed, more laid-back.

Kenshalo: Yeah. Inhibited their responses more or something like that. Yeah, could be. I don't remember. It was so long ago.

Meldrum: But this was all pretty much behavioral. You weren't doing... You weren't doing physiological reporting too.

Kenshalo: No, uh-uh. We did draw some blood from the animals and look at testosterone levels and correlated them. But other than that, it was strictly behavioral work. And that was kind of an offshoot of what the studies that Irwin Bernstein [sp.] had been doing at the field station, and it was a contract from Walter Reed Army Institute of Medicine, and those folks would come down and they were... I think we had the longest-running contract in the history of the Army. It went on for like 10 years, I think.

Meldrum: The Army trying to figure out what to do, how to train recruits?

Kenshalo: Yeah, how to make recruits out of either, whether they wanted higher-ranking or lower-ranking, yeah, or predict whether somebody was going to be a higher-ranking or lower-ranking.

Meldrum: Well, that's very interesting.

Who were you working with then?

Kenshalo: The primary guy was Brad Bunnell [sp.].

Meldrum: I don't know him at all, I guess.

Kenshalo: No. He's not a pain researcher. He's more of an endocrinologist. And he is--we used to do a lot of work with sexual behavior in hamsters.

Meldrum: Oh, that sounds really fascinating.

Kenshalo: Oh, yeah.

Meldrum: Okay. So this was mostly behavioral work.

Kenshalo: Yeah.

Meldrum: And you weren't... And can you tell me a little bit... I mean, I know that after you got your degree, or even before you got your degree, hadn't you moved to Texas?

Kenshalo: After I got my degree, yeah.

Meldrum: And you went to work with Bill Willis [sp.].

Kenshalo: Yep.

Meldrum: So tell me a little about how that transition occurred. I mean, obviously you were looking for a job.

Kenshalo: Yeah, or a postdoc, and I applied to a number of places. And Bill was the one that had backup money in case an NIH postdoctoral fellowship, and in those days there was a tremendous amount of money in Texas. They were being supported very nicely by the oil wells, the University of Texas system, and it was a great place to be at the time.

Meldrum: Yeah. I've never been there. You know, it's really--we haven't interviewed Bill Willis [sp.] and we should. I can't believe we haven't done that.

Kenshalo: Yeah.

Meldrum: Yeah. So tell me a little about the Marine Biomedical Institute?

Kenshalo: Yeah. We worked on crab-eating monkeys.

Meldrum: Yeah.

Kenshalo: There was actually quite a lot of marine research going on. There was another component of Bill Willis's [sp.] lab that they were looking at, sensory and motor interactions in stingrays and electrical discharges of stargazers and how that produced...

Meldrum: Really?

Kenshalo: Yeah. It was very interesting. Stingrays are fascinating creatures.

Meldrum: Yeah. They're really beautiful.

Kenshalo: They're really very tame, too. I mean, they'll just come up and take food right out of your hand.

Meldrum: Wow. Actually, I was just in Baltimore, at the aquarium, and they have a lovely stingray exhibit.

Kenshalo: Oh, do they?

Meldrum: Yeah. And they were. They were taking food and sort of... They were very mellow stingrays.

Kenshalo: Oh, yeah. They are, they are. They would come up to the side of the tank and beg for food.

Meldrum: Wow.

Kenshalo: We used to have huge, huge tanks with a tremendous number of stingrays in them.

Meldrum: So there were probably a number of lines of research that you could have done there.

Kenshalo: Oh, sure, yeah. There was a tremendous number.

Meldrum: So, what brought you into pain?

Kenshalo: Well, actually, I went to Bill's lab to look for cells in the spinal cord that responded to thermoreceptive stimuli, and he went on sabbatical about the time I was ready to start the project, and we started the project and it became apparent very quickly that that was not going to be a very productive effort. But there were a tremendous number of cells that responded to noxious heat, so you study what you can find.

Meldrum: _____.

Kenshalo: Yeah. So that was...

Meldrum: Wait a minute. You hadn't done any of this before, though. I mean, you hadn't been working on spinal cord before?

Kenshalo: Uh-uh, no. But there were lots of people, and you get integrated into the lab and, you know, after three or four months, you're perfectly capable of doing it on your own.

Meldrum: Oh, yeah. I just wondered where the interest came from. I mean, a lot of psychologists do basically behavioral research most of their lives and they never actually operate on anything.

Kenshalo: Yeah. Well, I had always been grounded in physiology from my father's lab in Florida State, and there was tremendous opportunities there. People were doing a lot of physiology and behavior there.

Meldrum: So you had this chance to, you actually had this chance to _____ graduate school.

Kenshalo: Yeah.

Meldrum: Okay. So you were in Bill Willis's [sp.] lab for quite some time.

Kenshalo: Yep, three years. It was a great place, great people. I think it was probably the best time to be there. He may not say that, but... I mean, in terms of the social atmosphere and the people that were there, social interactions, and plenty of money. Money was never an object.

Meldrum: Did each person have a separate project? You said you started...

Kenshalo: Yeah, mm-hmm, most people did.

Meldrum: So, how did you fund your project?

Kenshalo: What do you mean?

Meldrum: You developed your own individual project.

Kenshalo: Right. Well, as I say, I went there to do a specific...

Meldrum: _____ to do thermo _____? You told me all that. You must have had, you know, I mean, there was some original thinking in there somewhere.

Kenshalo: Well, I mean, nobody ever recorded... There was a tremendous amount known about how the peripheral thermoreceptors responded, but nobody ever recorded from. And I was really interested in what happens when this information is transmitted across synapses and how it's changed, and it didn't seem to me that it was kind of the Mount Castle [sp.] idea of just linear operators. I mean, there has to be more going on, and this providedthere was a tremendous amount of information on thermoreceptors, and it would be interesting to know how the second-order cells did.

Meldrum: Okay.

Kenshalo: And that's always been my primary interest of how the nervous system rearranges, whether it's thermoreceptive or nosiceptive information.

Meldrum: And Willis [sp.] was _____.

Kenshalo: Oh, yeah. Well, that was his lab, and the link was he'd been studying the spinothalamic tract for all those years and had never done any quantitative studies on temperature. And he was ready to really, ready to undertake that project at that time when I applied, so...

Meldrum: Okay. What was he like to work for?

Kenshalo: Oh, he was great. He was absolutely fantastic, easy-going. As long as you were getting data, then you couldn't do anything wrong, you know. He was great, laid-back, never got upset, never yelled, screamed, or... Except once.

Meldrum: What happened?

Kenshalo: Oh, there was a time when his wife had been in the laboratory adjusting the camera, and I hadn't gotten back to refocusing it. And we had one of the greatest experiments of all times and it was really just the consummate experiment we needed to finish up a project, and it turned out that all the film we had taken was out of focus and unusable.

Meldrum: Oh, God.

Kenshalo: So we had exchanged words about that. But that was about the only time he really got upset about something. And it turned out we had enough computer records that we could reconstruct what had happened.

Meldrum: Well, that's good.

Kenshalo: Yeah.

Meldrum: Okay. Now, I have a sense that computers really sort of had to be tinkered with a lot to do all this.

Kenshalo: Oh, yeah, yeah. It was real primitive.

Meldrum: Yeah. Those were the very early days. Nowadays, we just push buttons and, "Oh, look at this."

Kenshalo: Yeah, it comes out. Yeah. Back in those days, you had to have programmers and things like that to take care of everything.

Meldrum: And what about the monkeys? Was it... I mean, if you're tracing spinothalamic tracts, I mean, we're really talking about isolating the nerve fibers. Right? Not so much behavioral work?

Kenshalo: No, no behavioral work whatsoever.

Meldrum: Okay.

Kenshalo: No, uh-uh, just straight physiology.

Meldrum: But wasn't it hard then? I mean, could you not, for instance, have done that in some other animal? Aren't monkeys pretty expensive?

Kenshalo: Yeah, but there was plenty of money in Texas and...

Meldrum: Texas had lots of money.

Kenshalo: ...and we ran through Bill Willis's [sp.] grant in about the first three months of the year, and we were doing two monkeys a week, you know, chewing up...

Meldrum: Wow.

Kenshalo: Yeah.

Meldrum: That is a lot.

Kenshalo: Yeah. Except for neurosciences, I mean, it was a routine you got into. You slept on the weekends.

Meldrum: What was the most interesting work that you did or the most significant work? Or what do you remember the best?

Kenshalo: Oh, I think the thalamus project that we did was by far the most interesting. It was kind of a compromise. I'd always been interested in the cortex and the role of the cortex in pain. And I had--Steve Wise [sp.] and I had done some experiments together and looked at, looked for units in the cortex that responded to nosiceptive stimuli. And Bill made it known that he was not interested in that project and I probably should not be doing it, and so working in the thalamus was a compromise to that project. And I really thought at that point that was probably the best project I'd ever done, and the most useful.

Meldrum: _____.

Kenshalo: Yeah.

Meldrum: Now, are we talking about--we're talking about thalamic responses...

Kenshalo: To nosiceptive stimuli.

Meldrum: Rated stimuli?

Kenshalo: Mm-hmm.

Meldrum: Okay. I suppose it's something that was not very much... I mean, previously... Well, tell me what the previous thinking was.

Kenshalo: Well, I mean, we'd recorded a lot from the spinal cord and measured all the parameters and tracked out where all the spinothalamic tract cells go and what happens in the thalamus, how does the information change between the spinal cord and the thalamus.

Meldrum: Okay. So this did indicate that there was some modulation of the...

Kenshalo: Oh, yeah. There are tremendous numbers of modulations and transformations that occur between the spinal cord and the thalamus. The primary one is that the receptive fields become smaller.

It was also kind of interesting that none of the thalamic cells responded to nosiceptive cold stimuli, where they had in the spinal cord for some reason. You' d expect that that would be information that's passed on along. But the very striking one was that the receptive fields got much smaller. And, in addition, this tremendous input that spinothalamic tract cells appear to get from the viscera and muscles doesn't seem to be there in the thalamus at all. There doesn't seem to be that convergence that occurs. And that's also maintained at the level of the cortex. I don't know where that information goes, but it just seems to drop out. Things that never got answered.

Meldrum: Still hanging out there.

Kenshalo: Still out there. Yup, exactly.

Meldrum: Willis [sp.] didn't want to work in the cortex?

Kenshalo: No, because he felt it was too... He felt that his name was associated with the spinothalamic tract and the cortex was too far away from the spinothalamic tract.

Meldrum: But connected.

Kenshalo: Yeah. And he did allow... But we did backfire the thalamic cells from the cortex, which was very interesting and provided insights, at least to us-- maybe not to other people--where the nosiceptive information went in the cortex.

Meldrum: I should hope so, yeah.

Now, you've got--you did some work with serotonin.

Kenshalo: Oh, yeah. That was with a visiting scientist, yeah, Larry Jordan [sp.], who was there from Canada. It was his project. It was an ionephretic [sp.] study that we did looking at the response of spinothalamic tract cells to, spritzing serotonin on their cell bodies.

Meldrum: Okay.

Kenshalo: We just helped him with that, not...

Meldrum: Not.

Kenshalo: No. You get... All these studies required teams of people, and how interested you are in a particular project varies from project to project. Sometimes you're just acting as a technician and you're not particularly interested in the project, but this is what the lab is doing, so you help with it.

Meldrum: So you're _____ the other people.

Kenshalo: Yeah.

Meldrum: Okay. So I've got this note here that the spinothalamic tract is not a compact bundle but a pathway widely dispersed.

Kenshalo: In the intralateral and lateral quadrants. Yeah. Even in the dorsilateral quadrants.

Meldrum: And you talk here about wide-dynamic-range neurons and low-threshold mechanoreceptors and high-threshold mechanoreceptors. Now, ignorance here. I'm just trying to place all this. I mean, I first became acquainted with the idea of wide dynamic receptors by reading Ron's papers, but they were fairly well known. This idea of wide-dynamic-range neurons were fairly well known, others becoming known in the '70s. Do you remember?

Kenshalo: Mm-hmm, yeah.

Meldrum: Yes to which?

Kenshalo: I mean, they were, and the initial theory was that there was a nosiceptive-specific neurons that really transmitted information because they only respond to frankly noxious stimuli and so, therefore, then that left the idea of whether the wide-dynamic-range cells. And I think, from a number of studies, it became apparent. Still a contentious area about what the involvement of the nosiceptive-specific cells versus the wide-dynamic-range cells. But there was some data from Don Price's [sp.] lab that suggest in humans, that suggested, based on the refractory periods, that it was the wide-dynamic-range cells that might be responsible for transmitting the sensation of pain in humans. And it was kind of interesting, the initial... I think even Bill Willis [sp.], back in the middle '70s, kind of poo-pooed the idea that it was the wide-dynamic-range cells. But over the years there's been so much information collected that the wide-dynamic-range cells may really be the ones that transmit at least some portion of the sensory discriminative aspect of pain, that even he couldn't ignore it. And I think now that he and Ron probably are the leading proponents of the role of wide-dynamic-range cells in processing of nosiceptive information. But there are still specificity people out there that still refuse to acknowledge that wide-dynamic-range cells...

Meldrum: Yes. I have heard those _____.

Kensalo: Yeah, I bet.

Meldrum: Many, many times. Okay.

How aware were you of the pain field at this point? I mean, Willis was involved in the early days of the APS and certainly... I mean, you've known physiology all your life, so... But pain... I mean, my impression is that pain was at this point, in the '70s, only beginning to be thought of as a problem that people would actually spend their time working on.

Kenshalo: Yeah, I think that's true. There wasn't a whole lot known in the middle '70s about what was going on, and the competition wasn't tremendously fierce the way it is now, I don't think. You just kind of bump along, keep working along, and nobody else would scoop you. And I think the primary reason that Bill started working on spinothalamic tract, I think he started out to identify the response properties of all the tracts that went up and he got hung up on the spinothalamic tract and has stayed primarily with that to some extent. And he was interested in doing that because I think he thought that at that point, the variability in the cells, in the response of the cells, would be lower if he could identify their target areas, and so, therefore, identified cells would have more consistent patterns of response and physiological properties.

Meldrum: Anything else that happened while you were working there?

Kenshalo: He really just did it kind of serendipitously. He had a postdoc that wanted to do it, and then that kind of...

Meldrum: That kind of often happens.

Kenshalo: Yeah, yeah. And he just stayed with it.

Meldrum: _____.

Kenshalo: Mm-hmm.

Meldrum: So, anything else that you... This was... Okay.

So you're mostly now, I mean, you sort of changed... You were working on behavioral stuff, and now you're really working on sort of basic physiology.

So, anything else more you want to talk about in terms of your time with Willis [sp.]?

Kenshalo: No, I don't think so.

Meldrum: From there, you went to Barrow Neurological Institute in Phoenix. You wouldn't go north, would you?

Kenshalo: Now I know why.

Meldrum: No tennis.

Kenshalo: Now I know why.

Meldrum: Can't play tennis in the winter.

Kenshalo: I can't play tennis in the summer there.

Meldrum: That's true.

Kenshalo: It's torrid.

Meldrum: So, what took you to Phoenix, knowing how torrid it was?

Kenshalo: Offered me a good job.

Meldrum: And what exactly is it? I mean, this is a research job, right?

Kenshalo: Right. Barrow was a private neurological institution that was composed of neurosurgery, neurobiology, and neuroradiology. And they had, they needed neurobiology to support their residency programs, and they just hired a new person and they'd pumped a lot of money into establishing a research or revitalizing their research arm. And there was a neurosurgeon there named James Atkinson [sp.], who treated a lot of pain patients, and he unfortunately flew his plane into the side of a mountain. And one of his patients had donated--I've forgotten how much it was--it was $250,000 or $500,000 to establish a chair for pain research, so that was how I ended up there, and they were very generous in setting up a lab and providing equipment and people to help and things like that.

Meldrum: Okay. When you, in going there, I mean, you seem to have always stayed with research jobs. You didn't consider going to a place where you might teach.

Kenshalo: It just worked out that way.

Meldrum: It just worked out that way.

Kenshalo: Yeah. It wasn't a conscious decision, I don't think. It's just, the best jobs seemed to come along doing research, so that's what I went with.

Meldrum: In a couple of articles that you, at least that I found coming out of that work, you start... I mean, this is where I saw you start talking about sensory discriminative roles for specific neurons.

Kenshalo: Mm-hmm.

Meldrum: And, you know, a lot of your work seems to talk about the question of sensory discriminative roles. Can you sort of place that for me in the...

Kenshalo: Well, I think it's a lot easier to deal with--I was interested in pain as a sensory system and not the other components, the motivational affective components and the things that lead to the animal escaping prolonged stimulation. I was just interested in, how do you feel pain? When a painful stimulus occurs, how do you identify it as a painful stimulus, and what are the neurophysiological underpinnings of that sensation?

Meldrum: Okay. So, was this... This was physiological research that you were doing at the Barrow?

Kenshalo: Mm-hmm.

Meldrum: Again, operating, abstracting fibers from monkeys?

Kenshalo: Yeah. Primarily the cortex at that time.

Meldrum: Stimulate and see what the reactions were.

Kenshalo: Right, and where the cells were located and how they responded and that kind of...

Meldrum: That kind of stuff.

Kenshalo: Mm-hmm. Same stuff, only in a different place, in the brain.

Meldrum: In the brain.

Kenshalo: Angiographically.

Meldrum: Okay.

Kenshalo: The work I'd done with Bill Willis [sp.] in the thalamus kind of was the set, was the foundation for moving on to the cortex and looking in the primary somatosensory cortex.

Meldrum: When I first started looking at your work, I mean, supraspinal seemed to be the word that sort of came out of it. And that was, I mean, wasn't that really unusual? I mean, a lot of people have said to me that, you know, that their work has basically been spinal cord work and *the brain*. Everybody always says *the brain* is really sort of a tricky territory and hard to navigate in.

Kenshalo: Mm-hmm.

Meldrum: And do you find it so? And why do you think that is?

Kenshalo: It takes a little more effort than the spinal cord, but, no, I don't think so. I used to think you could make your living doing it, but, yeah, it's a little more difficult, because what happens is, at the level of the spinal cord, to record from the spinothalamic tract cells is easier because to a great extent the dorsocolumn system fibers are out of the picture. And by the time you get to the thalamus and cortex, all of that stuff, at least in my mind, is intermingled so that you have a tremendous number of cells that only respond to low-threshold stimuli, whereas that's not the case at the level of the spinal cord. But when you get to the thalamus and cortex, I mean, there are tremendous numbers of cells that only respond to low-threshold _____, and the cells that respond to noxious stimulation tend to get lost in the population of the other cells, low-threshold cells.

Meldrum: So really, you have to work... It sounds like...

Kenshalo: It's harder

Meldrum: ...it's really methodical, testing one cell after another after another after another after another, and...

Kenshalo: Exactly, mm-hmm.

Meldrum: It's hard.

Kenshalo: Well, it takes patience and perseverance, and stupidity, I guess.

Meldrum: So what did you like or not like about working at, aside from the heat thing?

Kenshalo: At Barrow?

Meldrum: Yeah.

Kenshalo: No technical support, none whatsoever. So I was doing all my own programming, all my own machining. I learned how to program computers, Apple computers, everything, and that took a lot of time. And that definitely cut the productivity rate. And there weren't any graduate students around and you could find some summer students to help, but it was primarily a technician, and there wasn't a whole lot of help at all.

Meldrum: Was it possible, I mean, you could have applied for grants to get _____?

Kenshalo: Oh, yeah, yeah. I had an NSF grant while I was there. But, you know, there are not the kind of students around that you're used to in Galveston, and graduate students.

Meldrum: Yeah. _____.

Kenshalo: Yeah, yeah.

Meldrum: They come around looking for jobs.

Kenshalo: And it took a while to get the first grant and, you know, I didn't feel it was really right at that point to bring somebody in when the future funding wasn't guaranteed, so by the time I got an NSF grant and got that going, it took a while to get a...

Meldrum: _____.

Kenshalo: What? Yeah.

Meldrum: It seems like you just get one grant, you immediately have to start writing and starting to try and get another one.

Kenshalo: Well, exactly, before you change jobs and come to NIH.

Meldrum: And so, you came to NIH.

Kenshalo: Yup. Came to NIH to...

Meldrum: Nineteen seventy-nine?

Kenshalo: Eighty-three.

Meldrum: Oh, 1983.

Kenshalo: Yeah.

Meldrum: _____ went to Barrow. Okay. So how did you come to NIH? Tell me the story.

Kenshalo: Well, I'd been doing all these things that were not particularly germane to doing science, like programming computers and doing surgeries and not having students, and Ron had a job that was open and had a lot of technical support and lots of people around and had an ongoing project. And I really thought at that particular point in time, the study I really needed to do was to be able to record from nosiceptive neurons in the cortex in an awake behaving monkey and be able to record their response properties. And he had all the psychophysics worked out.

Meldrum: Right. They'd already been working _____.

Kenshalo: Yeah. They'd already been doing it in the medullary dorsal horn.

Meldrum: Right, right. And so, what were you going to add on to this or what were you going to _____?

Kenshalo: Well, I wanted to do it in the cortex, and look at the correlation between the animals' behavior and the response of these cortical neurons to noxious stimuli.

Meldrum: Okay. So you lived in Bethesda...

Kenshalo: Mm-hmm.

Meldrum: ...and sort of settled down. Good tennis?

Kenshalo: Eh, okay. Pretty cold in the winter, but, you know.

Meldrum: Oh, yeah. I used to live in Minnesota.

Kenshalo: Oh, well. You've lost that, though.

Meldrum: Oh, yes, definitely. I couldn't even bear it anymore.

Kenshalo: So, how long had you been in L.A.?

Meldrum: I was in Los Angeles for four years. I've been here for two, so that's six years. But I was in New York, which was sort of in between.

Kenshalo: You didn't get spoiled by L.A.?

Meldrum: Yeah. L.A. is _____ spoiled by. If you can live with the traffic, it's...

Kenshalo: Well, Washington is going to rival it soon.

Meldrum: Tell me about it, tell me about it. And I don't suffer that very much because I never go into the city except on the Metro. Anyway, that's neither here nor there.

Who was there then? Kathy Bushnell [sp.]?

Kenshalo: Kathy. I took Kathy Bushnell's [sp.] job because she had married Gary Duncan [sp.] and Gary needed a job. Gary had been a postdoc in the lab when she was a staff fellow.

Meldrum: Right.

Kenshalo: And they--where'd they go? Montreal. Yeah.

Meldrum: Okay. And Bill Mexner [sp.]?

Kenshalo: Mexner [sp.]. He was a staff fellow in the lab at that particular point in time.

Meldrum: Well, so tell me... I mean, I've been reading about these experiments till they come out of your ears. I really do think they're interesting. I mean, they're just fascinating.

Kenshalo: The monkey experiments?

Meldrum: The monkey experiments. And certainly, I mean, you obviously had particular interest about recording from cortical cells, but you must have been interested in the way the monkeys' ability to do sensory discrimination.

Kenshalo: Well, I mean, you have to do a lot of different things to keep productive. I mean, these are very time-consuming experiments, so you do a lot of multiple. It's, you know, just like in Willis's [sp.] lab. You get involved in a lot of different things and help with a lot of different things, and there are team projects. So you may not be particularly interested in the project, for your own personal...

Meldrum: _____.

Kenshalo: Yeah, yeah, exactly.

Meldrum: What were the most interesting to you then?

Kenshalo: In terms of what?

Meldrum: In terms of those monkey experiments. What did you... Did you enjoy doing them? I mean, was this interesting to you?

Kenshalo: Well, I was...

Meldrum: Was this _____ stuff, stuff you already knew about?

Kenshalo: No. It was very laborious because... And the first couple of times we made it, looking for cortical cells that responded to noxious stimuli, didn't work. We were trying to do it in the arm and that didn't work, and we had, rather than persevere, I mean, there were so many technical problems you just didn't anticipate, like we had an arm restrainer for the monkeys and we were putting noxious heat on their arms, but every time they would lick on the spout, they would move their arm, and thousands of these low-threshold cells would discharge, so you could never identify what was responding to noxious heat and what was responding to the arm movement. And so we went back and did an acute study in the monkeys and looked at noxious responses in the face, where nobody else had done that, and tried to identify that. And then we went back into the monkey again. We did the project and it finally worked at that point.

Meldrum: It took a long time to train the monkeys.

Kenshalo: That was about--the whole project, to get to the point of recording, was about eight years, seven years.

Meldrum: Wow.

I have a paper here from 1989. I think you were the first author on this one. So you list...

Kenshalo: Yeah. That was the cortical project.

Meldrum: Is it? The _____ speed the small increase in stimuli imposed on noxious levels of thermal stimuli?

Kenshalo: Hmm?

Meldrum: That's what the conclusion was. Detection speed to small increments of stimuli is similar in monkey and man and is an accurate measure of the perceived intensity of painful stimuli.

Kenshalo: That's the *Journal of Neurophysiology*?

Meldrum: Yeah.

Kenshalo: Yeah, uh-huh.

Meldrum: You want to talk about that, about measuring the monkeys'...

Kenshalo: Well, what we did was we did the same experiments in both monkeys and humans using identical stimuli and asked the humans to detect and release a key just the way the monkeys did, and then compared their responses. Then, on top of that, we took those stimuli and asked the humans to magnitude-estimate their intensity and found out that the--then correlated the detection speeds with the magnitude estimates to the same stimuli and found out there was an almost identical match, so that the monkeys and humans perceive, in terms of their detection speeds, about the same thing, and they're all related. They're all an index of the measure of pain sensation, pain intensity. All these things have a reason, and there are many people that said, "Well, how do you know the detection speed is related to stimulus intensity?" So it seemed like a reasonable way to approach the problem.

And then we have all this eloquent data looking at the response of wide-dynamic-range cells and nosiceptive-specific cells in monkeys and how, from the medullary dorsal horn, and how they correlated with the animals' detection speed.

Meldrum: Certainly the wide-dynamic-range neurons seem to be more and more significant as you went through this.

Kenshalo: Oh, without a doubt, yeah, yeah. And there's a sub-population of wide-dynamic-range cells that look like they're even more significant. Just in terms of near-threshold pain stimuli from those studies, it would appear that it's the wide-dynamic-range guys that signal near-threshold stimuli.

Now, for really super-threshold stimuli, you can't discount that it might be the nosiceptive-specific, but those studies will never be done, I guess.

Meldrum: No, probably not. Was there any question about the work that you were doing with the monkeys, people asking... I mean, were there protesters sending you letters or...

Kenshalo: Oh, yeah. There were all kind of strange things. When I was here, it had calmed down a little bit, and then PETA really got to be active, and there were friends in the pain field, like Willie Dong [sp.] in Seattle and who actually had been picketed at their house. And they had done the same thing to Sharon Juliano [sp.], who worked over at Useless [sic] (USUHS?). But I took some steps to make sure that we were never bothered, and that is, you change the name on all your protocols so that it doesn't include the word pain in any point, and so you have totally benign-looking protocols and the titles for the protocols.

And then there were other instances where people would call and request to come to the lab, and they wanted to volunteer to work in the lab, and my response to this inquiries was always that, "Send me your CV and then I'll take a look at it and then we'll get back in touch."

About the same time, I was chairman of the Animal Care and Use Committee for the Institute as well, so I knew pretty well what was going on and when there would be protests, and we were pretty vigilant in the middle '80s about, particularly on animal liberation weekends, about monitoring what was going on in the lab and what was going on in the monkey room, before we moved to Building 49, because they were just in with the rest of the animals and there was not a tremendous amount of security. There was one lock between anybody that wanted to walk in off the street and the animals.

Meldrum: Yes, that is kind of _____.

Kenshalo: So, yeah, it was a major concern to have these animals with head plugs and...

Meldrum: _____.

Kenshalo: Yeah. But we were pretty cautious about maintaining a low profile, and we never had a tremendous amount of problems the way other people did.

Meldrum: Yeah. _____.

Kenshalo: It's an interesting time. I've seen the PETA people protesting out, and then they had parades through campus and everything like that. It was...

Meldrum: Well, there were a batch of them here last, early September, I guess.

Kenshalo: Were there?

Meldrum: Yeah. They were--the people put themselves into, I guess, cardboard cages and they were up and down Rockville Pike _____.

Kenshalo: Oh, yeah, yeah.

Meldrum: Fun to watch.

Kenshalo: Yeah. Their tactics haven't changed too much since then.

But it was a major concern because there were people, there were friends like Mac Hadley [sp.]--I think it's Hidley [sp.]--in England who had bombs placed under their cars. You know, you didn't know what would happen.

Meldrum: _____.

Kenshalo: Yeah.

Meldrum: Okay. So, what do you think was the most important or interesting thing that you did personally while you were doing these? And we're talking about the '80s now. I haven't moved into the '90s yet. I'm still in the '80s.

Kenshalo: Well, I mean, the study of looking at the correlation between nosiceptive neurons in the cortex and the animals' behavior, which there was never really a long manuscript published from that, but...

Meldrum: Yeah. That's pretty interesting. Have you got data that's not published?

Kenshalo: Oh, yeah, tremendous amounts of data that's not...

Meldrum: That might never get published?

Kenshalo: There's still hope. There's still two more papers that should be published. But getting comfortable in a new environment has taken a while.

Meldrum: Sure.

Kenshalo: But there's one that I worked on for 12 years.

Meldrum: Really?

Kenshalo: Yeah.

Meldrum: Doing what?

Kenshalo: It's a study looking at... I'm very persistent. I don't give up easily. It was--all I wanted to do was measure the frequency of nosiceptive neurons in the cortex in areas... Nosiceptive neurons aren't scattered uniformly across the cortex, so if you compare to the whole population of low-threshold cells, they'd probably be minuscule. But once you get into an area where there are nosiceptive neurons, there are tons of them. There are like four or five or six of them. And this study looked at how frequent you could find these neurons. And within an electrode track where you found one, the probability that you'll find another nosiceptive neuron is 50 percent. And this did not seem to really excite many reviewers to have this information published, for some reason. And the first couple of times, it came back saying there wasn't enough data, and then it's just... So finally it came back about a year ago, and I haven't made the revisions to it to send it back to the *Journal of Neurophysiology*. But it's been like pulling teeth to get them to...

Meldrum: _____ or something.

Kenshalo: That has never been said. But it just doesn't sit well with the rest of the field, for some reason. There are too many people that have... And I don't even know why it would threaten anybody, to tell you the truth, but it's been probably one of the chief reasons I changed fields. I got to be like M.A. and just totally frustrated, and to work on it was very aversive.

Meldrum: Yeah. I can certainly see that.

Aside from that, did you think that most of the neurons and the pain pathways have been sort of mapped? Do we really have a clear understanding of the signaling process and at least of what cells are involved?

Kenshalo: No, I don't think so. No. I think it's still virgin territory, you know. Still don't have any idea whether the cells in the cortex are really necessary, you know, or nobody's done really S2 at this point to know. And Bud Craig [sp.] has stated that it may be someplace else as well. So, no, I don't think that one's resolved at all. And then the big problem is--and I'm not even convinced that you can resolve those problems with FMRI or PET because the vast majority of nosiceptive neurons are in layers three and four, and compared to the rest of the neurons, you know, they're just insignificant. So I don't think you can really get enough activation to study these cells in a PET or FMRI.

Meldrum: _____ discriminate.

Kenshalo: Yeah, because they are buried and the signal is going to get lost as it comes out of the cortex, until somebody develops a way to look at only layer three or four and activation of those cells. And they're not the tremendously large cells to begin with. I mean, you can only record from these cells over a very limited area of brain, of electrode trajectory up and down. So they're pretty small cells to begin with, which is what you'd expect, you know, based on phylogenetically, it's the oldest system.

Meldrum: Right. But do we know--are people working in this area now?

Kenshalo: Not many.

Meldrum: No. I mean, believe me, I only had time to do more than sort of skim _____. It seems to me that PET is--people are really excited about PET now and...

Kenshalo: Bandwagon science.

Meldrum: Yeah. Everybody's really looking _____.

Kenshalo: If you're not doing PET, you're not doing the latest research, and FMRI and all that stuff.

Meldrum: It's obviously--you can do it in humans, which has some attraction.:

Kenshalo: Mm-hmm.

SIDE B

Meldrum: Okay. We're starting the second side of this tape.

You were saying it's expensive.

Kenshalo: Oh, yeah. I mean, the PET and FMRI, I mean, those are very expensive machines that they use. And I think they do reasonable jobs at answering those particular types of questions. But there are other questions that PET and FMRI can't answer, so...

Meldrum: So, tell me about working here. I mean, it sounds... The '80s seemed like a very exciting time to work here, a lot of interesting people.

Kenshalo: Mm-hmm. You mean in neurobi--NAB?

Meldrum: NAB, yeah.

Kenshalo: Yeah, the old NAB.

Meldrum: The old NAB.

Kenshalo: It was an interesting place to work, yes. Interacting with Ron was always a treat. There were lots of very heated discussions that were, if you think about it, it was totally amazing.

Meldrum: Was it valuable to work with people working in all these different areas and different fields, with the clinical people and M.A. and...

Kenshalo: You mean on the Ron thing?

Meldrum: Yes.

Kenshalo: No. I think Ron kept them separate. They weren't supposed to interact tremendously. That was his way of maintaining... Am I supposed to say things like this? Is this going to come back to haunt me?

Meldrum: Well, possibly, but you will be able to review this tape before it goes into the public domain.

Kenshalo: Oh. This is going in the public domain?

Meldrum: That's what the agreement says.

Kenshalo: Wow.

Meldrum: But you'll get to review it first.

Kenshalo: Oh. And delete?

Meldrum: If you want.

Kenshalo: Oh, okay.

Well, I mean, that's the way Ron maintained control. I mean, Ron wanted to be the big boss. There weren't going to be any other little bosses.

Meldrum: Okay. So separating them, divide and conquer. And...

Kenshalo: You didn't hear it from me.

Meldrum: Beyond these walls? No.

But was he--he was generally able to keep resources flowing in and people flowing in.

Kenshalo: Yeah. But I think it got harder and harder for him. I'm not even convinced at this point that the Institute has a real value for pain research.

Meldrum: Yes. Certainly not lately.

Kenshalo: And I think that was... Well, I think that was one of the reasons why he probably left. I mean, he wasn't getting the support, and things were getting tighter and tighter.

Meldrum: Yeah. I got that from him. It's just been more and more difficult.

Kenshalo: Yeah. And the Institute has never been very generous.

Meldrum: No. They seem to be a little stingy.

Kenshalo: But part of that was Ron's own fault. I mean, when they... I mean, you want the politics of the situation? They convinced Abner Notkins [sp.] to...

Meldrum: I don't even know who he is.

Kenshalo: He was a scientific director before Henning [sp.] that they finally kicked out.

Meldrum: Oh, okay.

Kenshalo: They convinced him to be scientific director, and he turned out to be a little megalomaniac.

Meldrum: Oh, dear.

Kenshalo: And he screwed them all.

Meldrum: So he was like mainly interested in himself?

Kenshalo: Oh, yeah, yeah. He was promoting himself as the next...

Meldrum: Next John Shannon [sp.] or, I mean Jim Shannon.

Kenshalo: Yeah, or something like that. Yeah. He was going to be the big power on campus.

Meldrum: Nobody's mentioned him to me at all.

Kenshalo: Yeah. And he--there's no doubt about it that he didn't keep Ron's budget growing the way his own was growing. And this is a very bizarre institute and it has... Only when you leave it do you find out how... You know, for instance... I'll put this on tape.

You know, most institutes give their employees bonuses at the end of the year that are mandated. This institute has never done that. That money has always disappeared. It has never gotten down to the people that it was intended.

Meldrum: That's very interesting. They probably go into the budgets of the director and so forth.

Kenshalo: Wherever.

Meldrum: Okay. So it doesn't seem as if this institute really had a commitment to pain, really.

Kenshalo: No, I don't think...

Meldrum: _____. Well, Ron came on when Seymour Preshover [sp.] was here.

Kenshalo: Yeah, and Maureen Iland [sp.].

Meldrum: Right, and he speaks warmly of them so _____.

Kenshalo: Yeah.

Meldrum: And then he stayed.

Well, unfortunately, pain--a lot of people still don't take pain seriously.

Kenshalo: I don't think NIH takes it seriously. Do you?

Meldrum: Oh, no. No.

Kenshalo: I mean, they've been here... How long have they been here, and they didn't have a pain consortium.

Meldrum: Yeah, yeah. If you look back in the minutes of various meetings, it's been more than six years now, eight years, I think, since the first mention was made of such, and money has been appropriated, yet somehow money never seems to, you know...

Kenshalo: Has money been appropriated?

Meldrum: Congress gives them money, yes, specifically... I think it was _____ for a consortium, but it was for some type of pain research. I'm quite sure that very little of it has filtered down here.

Kenshalo: No, I'm sure it hasn't. No.

Meldrum: It can be very frustrating.

Okay. What else can I ask you?

Kenshalo: I've told you everything I know.

Meldrum: Tell me, though... Tell me a little bit more about the cerebral cortex, exactly what you think it does in pain. I mean, we've talked endlessly about wide-dynamic-range neurons, but they're _____.

Kenshalo: I think it helps you make the initial distinctions of, the painful stimulus probably occurred and where it occurred, and it's not so concerned with the more chronic aspects of stimulation. For instance, I don't think it probably has a great deal, at least the primary somatosensory cortex, to do with long-term changes, or at least we could never prove that it had a real role in post-inflammatory pain. It does seem to mimic the plasticities, the same kind of plasticities in receptive-field sizes that you see in other, in the low-threshold system where, you know, all those studies by Mike Mersnick [sp.] and John Colstad [sp.] showed that if you amputate a finger, the receptive fields get large. Well, you know, you can still get the same activity-dependent state changes in a receptive field by injecting capsaicin into the receptive fields. Receptive fields get large and, you know, they become hyperresponsive in the level of the cortex. So I think it probably does have a real role to play, or at least it mimics the kinds of response properties you would think it would have if it were signaling changes in pain sensation, and there seems to be a parallel there.

Now, whether it really has a role or not, nobody knows. I mean, it's, you know, the...

Meldrum: _____.

Kenshalo: You can show that lesions of the somatosensory cortex, under certain circumstances, will influence pain behavior and pain sensation. But unlike...

Meldrum: Go ahead, I'm sorry.

Kenshalo: Unlike some of the other, like low threshold, you can't wipe it out entirely. So it's still an interesting problem, but I don't think--I'm not sure we'll have an answer anytime soon.

Meldrum: It'll be a hard thing to try to discriminate all the different cells that are involved.

Kenshalo: Mm-hmm.

Meldrum: And you said there hadn't been much work done in S2.

Kenshalo: Hardly any work in S2, hardly any work...

Meldrum: Are there pain neurons there?

Kenshalo: Well, you'd think there would be. I mean, if there's parallel processing or even serial processing or some combination, you would think that there would be. And certainly the pattern FMRI studies seem to indicate, under certain conditions, you can get activation of S2, maybe even more prominently than S1. So it's a tough ball game.

But, you know, there haven't been the studies done of lesioning primary somatosensory cortex and looking at various... We've tried to look at lesions, the influence of lesions on monkeys' ability to take noxious stimuli, and there are some changes. There are some changes in the monkeys' ability to discriminate, but, you know, they weren't tremendously profound, but there are other kinds of studies, you know, you need to do about whether the animal can localize a stimulus and tell you where it occurred on his body surface and those kinds of studies.

Meldrum: Yeah. They're just not getting...

Kenshalo: Not very sexy these days, but necessary, you know. At some point, somebody's got to do it.

Meldrum: Yeah, well, you would hope so, if somebody could come up with the money for them.

Kenshalo: Yeah. Well, and the problem is that they take tremendous amounts of time to do these things. Just to run three animals through a lesion study took us three years. So, I mean, it's a labor-intensive, prolonged study.

Meldrum: Yeah, it's hard work, and I think everyone thinks there's going to be new and faster solutions with humans and...

Kenshalo: Yeah. I think you're right. But, you know, the meaning of the message can't be found in the chemistry of ink.

Meldrum: That's very good. We'll definitely leave that part on the tape.

Kenshalo: Yeah. Oh, well.

Meldrum: Okay. So, I mean, the monkey studies sort of came to an end about the early '90s, around there?

Kenshalo: No. Well, there were some studies published as late... I had a pre-doc from Harvard that was the last, and I guess we finished up about '96-'97.

Meldrum: Yeah. That wasn't so long ago.

Kenshalo: Yeah, yeah.

Meldrum: And were you thinking about trying to develop some more cortical projects? Did you have projects in mind that have sort of been at the table?

Kenshalo: Oh, yeah, definitely, looking at more post-inflammatory kinds of pain, pain studies, and then the cortex. And even--I was going to collaborate with Sokoloff [sp.] and look at some 2TT studies to see if we couldn't find any other correlates of post-inflammatory pain and the response of cortical neurons and kind of do a screening of the whole nervous system to see if what was happening, whether the cortex just wasn't activated or what, and then the next step was to do optical imaging techniques on the cortex to really get an idea of the distribution of nosiceptive neurons in the cortex. And that camera is sitting right there. That's what that box is.

Meldrum: Oh, is that what that box is?

Kenshalo: If you want a really fancy black-and-white camera, there it is.

Meldrum: Is that what it is? Maybe you should hang on to it. There was a lot of stuff on the floor. I notice they've finally taken it away. I kept kicking it. _____ computer.

Kenshalo: Yeah. Oh, yeah. I brought it back and...

Meldrum: Well, so tell me about... Let's see, how do I phrase... I mean, there was... About '96, Ron left and went to Baltimore.

Kenshalo: That was earlier, wasn't it? Didn't he leave in '95, '94?

Meldrum: I had '96, but, I mean, I'm just remembering it, actually. It's not really significant.

Kenshalo: No. I think it was earlier than that.

Meldrum: Okay. He departs.

Kenshalo: Okay. Yeah.

Meldrum: So, sort of characterize these last few years. It sounds like it's been quite a bit of a struggle for you.

Kenshalo: Well, there was a pre-doc from Harvard who was on loan, and most of the work went into getting him finished in a Ph.D. He was part of the Mark Program.

Meldrum: What was his name?

Kenshalo: Sholes [sp.], Murray Sholes [sp.]. And he--so there was a great deal of effort that went into getting him finished during that period of time.

Meldrum: Okay. But your own work was not getting funded or was getting...

Kenshalo: Well, I mean, there just wasn't a whole lot of help once he left. There wasn't--I didn't have anybody at that particular point. I got caught in the budget squeeze and I'd always supported postdocs on NIH postdoctoral fellowships, and for some reason they decided you couldn't do that anymore, and since I didn't have a line item in the budget for a postdoc, I lost it, and it took a while to get it back. So I sat for two years without any help, essentially.

Meldrum: That's pretty _____.

Kenshalo: Yup.

Meldrum: So, when did you decide to go to CSR?

Kenshalo: Oh. Well, that was kind of an interesting experience. Dave Thomas [sp.] sent me an e-mail, and I hadn't been in real close contact. Dave Thomas [sp.] had been in the lab as a postdoc. I mean, he was pre-doc and a postdoc for about 10 years. He was almost a permanent fixture, and he was a program person in NIDA. And I hadn't really been conversing with Dave at all, and out of the blue he sent me an e-mail saying that there was a position open for somebody to do, run the pain study section over at CSR, and I kind of tucked it away and then, you know, got to thinking about it more and more, and it seemed like... And I'd almost done it in the middle '90s, but it seemed like the thing to do. It wasn't tremendously satisfying doing the science anymore, and I shouldn't have waited that long to do it. It's been a lot of fun to see it from the other side.

Meldrum: Yeah, I imagine. I think it would be very interesting, actually, and exciting.

Kenshalo: Yeah, it is, it is. In some way, I mean, it's just really nice to do something different after that period of time. And I like interacting with people on the study section. It's exciting seeing the applications come through, and the subtleties of influencing how things are reviewed is really fascinating. It's a great system we have, actually.

Meldrum: Yeah. Despite its many, many flaws, there's probably... I mean, it's hard to think of a better system in a lot of ways.

Kenshalo: Exactly, exactly. I agree with that a hundred percent. And it's, you know most people get a fair shake, I think.

Meldrum: Well, I think that's a tremendous effort to give people a fair shake, even though... That's been my impression. I've been sort of tangentially involved with a lot of different study sections in different ways.

Kenshalo: But you have to remember, 80 percent of the people are going to be unhappy right off the bat.

Meldrum: Yeah, of course they are.

Kenshalo: Som, you know, you start with that bias and... I think most people aren't too contentious. There are a few.

Meldrum: The system _____. The system is...

Kenshalo: Yeah, set up so that only 25 percent are going to get the payoff. Right?

Meldrum: Right. And if you look at the statistics, it's... There's a book that a historian here at NIH wrote a couple of years ago called *A Half Century of Peer Review*, and if you just sort of, you know, graph the number of applications that have been coming in against the budget, you can see how impossible a situation it's been.

Kenshalo: Yeah. Yeah, exactly.

Meldrum: The more money that was appropriated, the more money, you know... And everyone that was funded back in the '50s and '60s then started training all these postdocs, and, of course, they all wanted to be funded too. So it grew in a geometric sequence _____. It's very difficult.

Have you seen a lot of innovative work, do you think, or is...

Kenshalo: You mean in pain?

Meldrum: Yeah. Well, I'm only interested in pain.

Kenshalo: Well, do you know, it's interesting. I don't think... There's some, certainly, but the real innovative work is really in smell, is in olfaction. They are so far ahead of everybody else in being able to clone the receptors and knock out specific parts of the receptors, and they know... It's just--it's fascinating how far behind pain is compared to...

Meldrum: Whoa. Now, is smell equally complicated?

Kenshalo: Oh, I think it's more complicated. I mean, just think. You've got different receptors and different volatile substances, and various parts of the olfactory mucosa signal various kinds of smells. It's fascinating how much farther they are ahead. And mapping the genome for it. It's just incredible.

Meldrum: Gosh, that's a whole new area.

Kenshalo: I know. You know, that's part of my study section, is the taste and olfaction, and those folks are just...

Meldrum: They're really going to town.

Kenshalo: Yeah, yeah. You know, it's not my particular bias to have everything molecular, but in terms of what they're doing with genes and the molecular biology of the olfactory system, it's astounding.

Meldrum: Wow, that's really interesting.

Kenshalo: Yeah. I mean, it makes pain seem like we're... Those folks are back in the dark ages, you know.

Meldrum: The medieval period.

Kenshalo: Or maybe the early '50s, not medieval. But, I mean, it's just, it's incredible.

Meldrum: I suppose the research is probably a little bit more easy to do. I mean, it's probably easier to get _____.

Kenshalo: Yeah. You've got the olfactory epithelium sitting right there rather than the receptors buried in the skin. But still, I mean, they're just--it's incredible.

Meldrum: Fascinating. Okay.

Well, this is something, you know, I had a talk with about... I guess it was a talk I gave to some historians, and I was talking about pain as it was sort of explained to me, as a sensory system, and talking about the complexity of pain in comparison to, for instance, what we know about visual, the visual system and about how we learn to discriminate visually and how that's a learning aplastic process. And so I was drawing analogies back... And someone raised the question about whether or not pain wasn't more like hunger or thirst. And, I mean, Pat Wohl [sp.] has talked about that, too, as well, hasn't he? I mean, if you were going to think about pain, do you see pain as primarily a sensory system?

Kenshalo: Well, I do, but that was always my bias because I was interested in sensory physiology rather than viewing it as a primordial system like hunger and taste, although it certainly has that component.

Meldrum: Yeah.

Kenshalo: But it's also got the sensory component as well. It ought to operate the way any other sensory system operates.

Meldrum: Yeah. Well, it should. And the other machinery is really kind of a different system, the affective and motivational _____ and motivational, which can react to any kind of strong, what do you want to call it, noxious or aversive sensation.

Kenshalo: You'd think so.

Meldrum: Well, I would think so, but _____. I'm just a historian. I just take notes.

Kenshalo: You've probably got a better overview of the pain field now as anybody.

Meldrum: Oh, I get _____. I learn more all the time, but it's really _____. There's so much going... I mean, you say that the research is sort of backwards, and it is. I suppose you're right. But there's just so much to keep track of in all these different fields.

Kenshalo: Well, that's true.

Meldrum: What about where the most interesting work is being done nowadays in pain? If you were going to...

Kenshalo: You mean the area or what?

Meldrum: Well, let me ask that question a different way. Suppose some student or undergraduate or some relatively young person came to you and, you know, maybe he's been doing some early, some starting research on neurophysiology. Would you _____.

Kenshalo: Well, I think you'd have to send him to the molecular people and study the molecular biology of...

Meldrum: Well, that's really where the...

Kenshalo: Well, that's where it's heading, unfortunately.

Meldrum: You're not really happy about that, though.

Kenshalo: No. Well, I think that's, you know, certainly an important area. I just don't think everything else should be excluded just because somebody's not doing molecular biology, which seems to be an emphasis at NIH, that they're sciences and worthwhile.

Meldrum: _____ NIH.

Kenshalo: Yeah. I mean, you know, I've never been a particular proponent of bandwagon science. There are other questions that are equally important that can't be answered with molecular techniques, and I don't think the molecular biologists know diddly-squat about sensation and unless you can tie it to sensation...

Meldrum: Right, what are we talking about?

Kenshalo: Right. I mean, there might be a minute, trivial, insignificant event, you know.

Meldrum: Yeah. Well, you do sort of see that sometimes in talking with, listening to some of the conversations here, which are truly fascinating, you know, about pre-pro... I can't even pronounce it.

Kenshalo: Pre-protechikinens [sp.] and...

Meldrum: Yeah, you know pre-dinorphin [sp.], pre-prodinorphin [sp.], and pre-enkeflin [sp.], and, you know, they really get beautiful results, not quite fascinating.

Kenshalo: And then you find out it doesn't have any; it doesn't correlate with the pain.

Meldrum: _____. Yeah.

Kenshalo: The pain and inflammation at all.

Meldrum: You know, it could be some side process...

Kenshalo: Yeah.

Meldrum: That we're not too clear on.

Kenshalo: _____ for the system.

Meldrum: Are there any places, then, that are doing really interesting neurophysiology now?

Kenshalo: Just straight neurophysiology? I think that Bill Willis [sp.] still is doing a lot, but I haven't kept up with, the past couple of years, what he's been doing.

Meldrum: I haven't either, so I _____.

Kenshalo: Yeah. So I don't know. You know, I still like the Fred Lynns [sp.] and recording in human. I think it's important, and he's certainly the leader in that field. I think Clifford Wolf [sp.] is probably near the forefront of the field, I would suspect, given his factory and...

Meldrum: His factory _____.

Kenshalo: And, you know, he certainly has the underpinnings of being able to do some behavior and physiology and molecular biology. So I guess that would be the lab I would say probably that has all the tools to certainly make some interesting...

Meldrum: Yeah. They certainly have the resources to do that.

Kenshalo: Mm-hmm.

Meldrum: Certainly one of the truisms of, what do you want to call it, cliches of the pain field is the importance of having basic scientists keep in full touch with clinicians and vice versa. Now, you've been primarily--you've been a basic scientist. Do you see that as important? Do you have any memories of talking to clinicians that were significant, or is that just a...

Kenshalo: Well, I mean, that was what NAB was supposedly about. Now, whether or not there was all that much interaction was questionable, I think.

Meldrum: Well, it's kind of hard to promote unless there's something really to talk about.

Kenshalo: Yeah. I didn't think there was... There were individual people in the program who certainly flitted back and forth between basic science and the clinical, you know, people like Ken Hargreaves [sp.] and those folks. But in terms of the core group of basic scientists, I don't think there was a whole lot of interaction between them and the clinical people, for instance. I think there was much more interaction with the clinical people coming to see what, getting ideas from the basic scientists than the basic scientists going to Mitchell Max [sp.] or Ray Dione [sp.] to see what they were doing. As a cynic, I think that would be my viewpoint.

Meldrum: Okay.

Kenshalo: I think that's a very difficult proposition.

Meldrum: It is difficult. It's hard to do. I mean, it sounds nice in theory.

Kenshalo: But practically, I'm not sure.

Meldrum: Okay. So, as you look back over all this work that you did, tell me again, what do you think is the most important thing that you personally contributed.

Kenshalo: If I ever get that organization paper, that will be the...

Meldrum: Well, they need to write that up.

Kenshalo: Yeah, it needs to be done.

Meldrum: Yeah. Okay.

Kenshalo: I mean, I think that'll be the only study of its kind.

Meldrum: Okay. Well, still something to look forward to, then.

Kenshalo: Let's hope.

Meldrum: Okay. We'll conclude this interview. I'm not sure exactly what time it is now.

Kenshalo: Eleven twenty-five.

Meldrum: Eleven twenty-five. It's still March the 17th. And thank you very much.

Kenshalo: Oh, my pleasure.